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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/539,560

06/17/2005

Toshifumi Yamaki

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EXAMINER

RAMIREZ, DELIA M

ART UNIT

PAPER NUMBER

1652

NOTIFICATION DATE

DELIVERY MODE

02/20/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/539,560	<b>Applicant(s)</b> YAMAKI ET AL.	
	<b>Examiner</b> DELIA M. RAMIREZ	<b>Art Unit</b> 1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 December 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 102-116 is/are pending in the application.
- 4a) Of the above claim(s) 114-116 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 102-113 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 June 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/9/08</u> .   | 6) <input type="checkbox"/> Other: _____                          |

Art Unit: 1652

## **DETAILED ACTION**

### ***Status of the Application***

Claims 102-116 are pending.

Applicant's cancellation of claims 1-9, 23-27, 35-39, 50-101, addition of new claims 102-116, amendments to the title and the specification, as submitted in a communication filed on 12/9/2008 are acknowledged.

New claims 114-116 are directed to isolated host cells, which are encompassed by the subject matter of Group D as described in the restriction requirement mailed on 9/26/2007. Claims 102-113 are at issue and are being examined herein. Claims 114-116 are withdrawn from consideration as being directed to non-elected subject matter. Claims 102-113 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on 12/9/2008 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Specification***

2. The previous objections to the title and abstract are hereby withdrawn in view of applicant's amendment of the title and the submission of an amended abstract on 6/17/2005.

Art Unit: 1652

***Claim Objections***

3. Claims 102-103, 106-110, 113 are objected to because “th”, “nd” and “st” next to the numbers recited should be in superscript. Appropriate correction is required.
4. Claims 102, 106-107, 109, 113 are objected to due to the recitation of “peptide of SEQ ID NO: 1/2” because SEQ ID NO: 1 and 2 represent proteins having 205 and 223 amino acids, respectively, thus not being considered peptides. It is suggested the term be amended to recite “polypeptide of SEQ ID NO: 1”. Appropriate correction is required.
5. Claim 105 is objected to due to the recitation of “wherein the  $\beta$  subunit is the amino acid sequence of SEQ ID NO: 2” because an amino acid sequence is a graphical representation of the order in which amino acids are arranged in a protein whereas the  $\beta$  subunit is a protein. Thus a protein is not the same as an amino acid sequence. It is suggested the term be amended to recite, for example, “wherein the  $\beta$  subunit consists of the amino acid sequence of SEQ ID NO: 2” or “wherein the  $\beta$  subunit has the amino acid sequence of SEQ ID NO: 2”. Appropriate correction is required.
6. Claim 109 is objected to due to the recitation of “415t” and “val”. The terms should be amended to recite “41th” and “Val”. Appropriate correction is required.
7. Claim 110 is objected to due to the recitation of “at positions 200<sup>th</sup> to Glu, or”. It should be amended to recite “at position 200<sup>th</sup> to Glu, or..”. Appropriate correction is required.

***Claim Rejections - 35 USC § 112, Second Paragraph***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
9. New claims 102-113 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

Art Unit: 1652

10. Claims 102 and 109 (claims 103-108, 110-113 dependent thereon) are indefinite in the recitation of “variant of the peptide of SEQ ID NO: 1 wherein the amino acid sequence of said variant of the peptide of SEQ ID NO: 1 is substituted at positions 36<sup>th</sup> to Met....” and “wherein said amino acid of variant of the SEQ ID NO: 2 is substituted at positions 10<sup>th</sup> to Asp....” for the following reasons. As written, it is unclear if the mutations listed are going to be made to the variant or if the mutations are going to be made to the polypeptides of SEQ ID NO: 1/2 to obtain the variants. In addition, the term “wherein said amino acid of variant of the SEQ ID NO: 2” in claim 109 is unclear and confusing because there is no antecedent basis for “said amino acid of variant”. Also, the term appears to be grammatically incorrect. For examination purposes, it will be assumed that claim 102 recites “variant of the polypeptide of SEQ ID NO: 1, wherein the amino acid sequence of SEQ ID NO: 1 has been substituted at position 36<sup>th</sup> to Met; 71<sup>st</sup> to His; 148<sup>th</sup> to Asp; 204<sup>th</sup> to Arg, Lys, Trp, or Thr; 148<sup>th</sup> and 204<sup>th</sup> to Asp and Arg, respectively; or 36<sup>th</sup>, 148<sup>th</sup>, and 204<sup>th</sup> to Met, Asp, and Arg, respectively. Claim 109 will be interpreted as reading “wherein the  $\beta$  subunit is a variant of the polypeptide of SEQ ID NO: 2, wherein the amino acid sequence of SEQ ID NO: 2 has been substituted at position 10<sup>th</sup> to Asp, Glu, Trp, Gly, Tyr or Cys; 32<sup>nd</sup> to Gly; 37<sup>th</sup> to Thr.....or 127<sup>th</sup>, 160<sup>th</sup> and 186<sup>th</sup> to Ser, Trp, and Arg, respectively.”. Correction is required.

11. Claims 103, 106-108, 110, 113 are indefinite in the recitation of “the X subunit which is substituted amino acid at position ....is further substituted amino acid at position ..” and “wherein the X subunit is substituted at position....” because it is unclear if the claims require modifications to the X subunit at the recited positions or if the X subunit is the result of the polypeptide of SEQ ID NO: 1 or 2 being modified at the recited positions. See above for explanation of similar issue. In addition, the term “which is substituted amino acid at position(s)” is grammatically incorrect. For examination purposes, it will be assumed that claim 103 reads “the amino acid sequence of SEQ ID NO: 1 has been substituted at positions 36<sup>th</sup> and 126<sup>th</sup> to Met and Tyr, respectively; 36<sup>th</sup>, 6<sup>th</sup>, and 126<sup>th</sup> to Met, Thr and Tyr,

Art Unit: 1652

respectively; or 71<sup>st</sup>, 19<sup>th</sup> and 126<sup>th</sup> to His, Val, and Tyr, respectively”, and claim 110 reads “the amino acid sequence of SEQ ID NO: 2 has been substituted at positions 51<sup>st</sup> and 108<sup>th</sup> to Val and Asp, respectively; 118<sup>th</sup> and 200<sup>th</sup> to Val and Glu, respectively;.....”. Claim 106 will be interpreted as reading “wherein the amino acid of SEQ ID NO: 1 has been substituted at positions 36<sup>th</sup>, 148<sup>th</sup>, and 204<sup>th</sup> to Met, Asp, and Arg, respectively, and wherein the  $\beta$  subunit is a variant of the polypeptide of SEQ ID NO: 2, wherein the amino acid sequence of SEQ ID NO: 2 has been substituted at positions 41<sup>st</sup>, 51<sup>st</sup>, and 108<sup>th</sup> to Ile, Val, and Asp, respectively”. Similar language will be used to interpret claims 107-108, 113. Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. New claims 102-113 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. This rejection was applied to now canceled claims 1-9, 55, 72, 77-84 and is withdrawn by virtue of Applicant's amendment. However, it is now applied to new claims 102-113 for the reasons of record and those set forth below.

15. Applicant argues that the claims have been amended such that their full scope is fully supported by the examples set forth in the specification.

16. Applicant's arguments and amendments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 102-113. While the amendments define specific substitutions which the Examiner has interpreted as substitutions made to either the polypeptide of SEQ

Art Unit: 1652

ID NO: 1 and/or 2, the claims still encompass a genus of variants which is not limited with regard to other modifications or substitutions that can be made to the polypeptides of SEQ ID NO: 1 and/or SEQ ID NO: 2 in addition to those specifically indicated in the claims. This is evidenced by the fact that, for example, claims 103, 106, 107, 108 requires additional modifications in addition to those set forth in independent claim 102. A similar situation is seen with claims 110, 113 and independent claim 109. Clearly the claims are not intended to be limited solely to the substitutions recited. As such, the variants recited can have essentially any structure so long as the recited substitutions are present. Furthermore, claims 102-103 encompass any  $\beta$ -subunit having any structure, whereas claims 109-110 encompass any  $\alpha$ -subunit having any structure. Therefore, claims 102-103 and 109-110 encompass nitrile hydratases wherein the structure of one of the subunits is completely unknown and the structure of the other subunit is essentially unknown, whereas the remaining claims encompass nitrile hydratases where the structure of both subunits is virtually unknown. Thus, for the reasons extensively discussed in the previous action mailed on 7/9/2008, the teachings of the specification do not adequately describe a genus of proteins having either any structure or essentially any structure.

17. New claims 102-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a nitrile hydratase comprising an  $\alpha$  and a  $\beta$  subunit, wherein the  $\alpha$  subunit is a variant of the polypeptide of SEQ ID NO: 1 which differs from the polypeptide of SEQ ID NO: 1 solely by amino acid substitutions at positions 6, 19, 36, 71, 126, 148, and/or 204, and wherein the  $\beta$  subunit is a variant of the polypeptide of SEQ ID NO: 2 which differs from the polypeptide of SEQ ID NO: 2 solely by amino acid substitutions at positions 10, 20, 21, 32, 37, 41, 46, 48, 51, 72, 108, 118, 127, 146, 160, 186, 200, 212 and/or 217, does not reasonably provide enablement for a nitrile hydratase having  $\alpha$  and a  $\beta$  subunits, wherein said subunits have either any structure or are variants of the polypeptides of SEQ ID NO: 1 or 2, respectively, wherein said variants are the result of any number of modifications to the

Art Unit: 1652

polypeptides of SEQ ID NO: 1 or 2, including those recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

18. This rejection was applied to now canceled claims 1-9, 55, 72, 77-84 and is withdrawn by virtue of Applicant's amendment. However, it is now applied to new claims 102-113 for the reasons of record and those set forth below.

19. Applicant argues that the claims have been amended such that their full scope is fully supported by the examples set forth in the specification.

20. Applicant's arguments and amendments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 102-113. As stated above, the Examiner acknowledges the amendments made to the claims but as interpreted, the claims still encompass a genus of variants where the subunits can have either any structure or essentially any structure. See extensive discussion of scope above. Neither the specification nor the art provide a structure/function correlation which would allow one of skill in the art to envision the structure of any  $\alpha$  and/or  $\beta$  subunits of a nitrile hydratase nor is there any teaching or suggestion as to additional structural modifications that can be made to the polypeptides of SEQ ID NO: 1 and 2 beyond those specifically disclosed in the specification, that would result in variants of the polypeptides of SEQ ID NO: 1 and 2 that, when in contact with each other, would display nitrile hydratase activity. Thus, for the reasons extensively discussed in the Non Final action mailed on 7/9/2008, one of skill in the art would have to go through the burden of undue experimentation to enable the entire scope of the claimed genus of proteins. Therefore, one cannot reasonably conclude that the full scope of the claimed invention is enabled by the teachings of the specification and/or the prior art.



Art Unit: 1652

***Claim Rejections - 35 USC § 102***

21. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

22. Claims 1-2, 4-8, 55, 72, 77-82-84 were rejected and new claim 109 is rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al. (Biochimica et Biophysica Acta 1129:23-33, 1991; cited in the IDS).

23. This rejection has been discussed at length in the Non Final action mailed on 7/9/2008.

24. This rejection as applied to now canceled claims 1-2, 4-8, 55, 72, 77-82, 84 is withdrawn by virtue of Applicant's amendment. It is noted that new claims 102-108 and 113 are not anticipated by the instant reference because claims 102-108 require specific substitutions at positions 36, 71, 148, 204 of SEQ ID NO: 1, and claim 113 requires specific simultaneous substitutions at positions 6<sup>th</sup>, 10<sup>th</sup> and 126<sup>th</sup> of SEQ ID NO: 1. Thus, while the instant reference teaches substitutions at positions 36, 71, 148, 6, 19 and 126 of SEQ ID NO: 1, the reference fails to teach the specific amino acids with which the substitution is made. However, the rejection is applied to new claim 109 for the reasons set forth below.

25. Applicant argues that the examiner's position is incorrect because either using uniform number matching or conserved motif matching, the same amino acid change will occur accidentally when one focuses at a particular position. However the amino acid sequences are not the same because applicant's protein and the protein of Kobayashi et al. are from different organisms.

26. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claim 109. It should be noted that when determining patentability, the examiner has used the broadest reasonable interpretation of the claims and determined whether the product claimed and that of the art have the same structural/functional characteristics. In the instant case, the subunits of the protein claimed are defined by structural and functional limitations. Thus, so long as the structural and functional limitations are met, whether the protein of the art and that of the invention are derived from

Art Unit: 1652

different organisms, or whether the amino acid substitutions occur accidentally or are man-made is irrelevant. Claim 109 is directed in part to any nitrile hydratase wherein said nitrile hydratase comprises an  $\alpha$  and a  $\beta$  subunit, wherein the  $\alpha$  subunit can have any structure and the  $\beta$  subunit is a variant of the polypeptide of SEQ ID NO: 2 wherein said variant has substitutions at positions 37, 118 or 186, wherein the amino acid at position 37 has been substituted with leucine, the amino acid at position 118 has been substituted with alanine, or the amino acid at position 186 has been substituted with serine. As previously discussed, the scope of the claims is such that there is no limit to the number of substitutions or modifications that can be made to the polypeptides of SEQ ID NO: 1 or 2. All that is required by the claims is that the specific substitutions be present. In the instant case, the  $\beta$  subunit of Kobayashi is a variant of the polypeptide of SEQ ID NO: 2 wherein said variant is the result of deleting the last four amino acids of the polypeptide of SEQ ID NO: 2 and substituting several amino acids within SEQ ID NO: 2 from amino acids 1-229, including the following substitutions: the amino acid at position 118 of SEQ ID NO: 2 has been substituted with alanine and the amino acid at position 186 has been substituted with serine. If consideration is given to conserved motifs, the  $\beta$  subunit of Kobayashi et al. is a variant of the polypeptide of SEQ ID NO: 2 wherein the amino acid of position 37 of SEQ ID NO: 2 has been substituted with leucine. See alignments and discussion provided with the previous Office action. Therefore, the nitrile hydratase of Kobayashi et al. anticipates the instant claim as written.

***Allowable Subject Matter***

27. Isolated nitrile hydratases which comprise an  $\alpha$  and  $\beta$  subunit, wherein the  $\alpha$  subunit is a variant of the polypeptide of SEQ ID NO: 1 which differs from the polypeptide of SEQ ID NO: 1 solely by the specific substitutions recited in the claims, and wherein the  $\beta$  subunit is a variant of the polypeptide of SEQ ID NO: 2 which differs from the polypeptide of SEQ ID NO: 2 solely by the specific substitutions recited in the claims appear to be allowable over the prior art of record.

***Conclusion***

28. No claim is in condition for allowance.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez, Ph.D., whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashaat Nashed can be reached on (571) 272-

Art Unit: 1652

0934. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Delia M. Ramirez/

Delia M. Ramirez  
Primary Patent Examiner  
Art Unit 1652

DR  
February 18, 2009